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Potential impacts of climate change on veterinary medicinal residues in livestock produce: an island of Ireland perspective

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Abstract

Residues of veterinary medicines are a food safety issue regulated by European legislation. The occurrence of animal diseases necessitating application of veterinary medicines is significantly affected by global and local climate changes. This review assesses potential impacts of climate change on residues in food produced on the island of Ireland. Use of various classes of veterinary drugs in light of predicted local climate change is reviewed with particular emphasis on anthelmintic drugs and consideration is given to residues accumulating in the environment. Veterinary medicine use is predicted to increase as disease burdens increase due to varied climate effects. Locally relevant mitigation and adaptation strategies are suggested to ensure climate change does not adversely affect food safety via increasing drug residues.

Introduction

Chemical contamination of food is a wide ranging topic encompassing many exogenous chemicals which may or may not be harmful to the consumer. Broadly speaking, contaminants may be categorised as agrochemicals (primarily residues of veterinary medicines and pesticides), environmental contaminants (primarily heavy metals, persistent organic pollutants and natural toxins) and processing contaminants (from cooking, processing or packaging). Recent and future climate change will have significant impacts on the dynamics of most of these routes of contamination. The nature of these impacts will

differ across geographical regions, making a review of climate change and chemical food safety on a global scale potentially too vague and speculative. Focussing upon a distinct geographical area such as the island of Ireland (Iol; comprising the Republic of Ireland and Northern Ireland, the latter being part of the United Kingdom) may highlight particular issues which can be applied or discounted in other regions.

A review of such an amorphous field and its interaction with climate change and food safety with a specific Iol perspective must necessarily focus on the most relevant threats to the consumer of foods originating on Iol, considering which chemical contaminant threats may reasonably be expected to have a predictable climate-related function, which are most relevant to the agri-food industries as practiced on the island, and which may be amenable to intervention strategies at the local level. This review addresses the major agri-food livestock sectors on Iol and assesses how the chemical safety of livestock produce may be affected by climate change. It focuses specifically on the classes of veterinary medicinal drugs which are widely administered and are integral to local livestock systems and whose potentially harmful residues in food are currently controlled by European Union (EU) regulations.

There is a general move within the EU towards reducing veterinary drug use (routine use for growth promotion is banned), accompanied by growing organic and extensive production systems and improving biosecurity and vaccination programmes. However, the use of medicines to maintain animal health and welfare, thereby improving production, remains a necessity. Controlling residues of these medicines in food continues to be important for consumer safety.

The effect which climate change in the 21st century may have on veterinary drug residues in food is primarily a question of how climate change will affect diseases of farm animals which necessitate administration of those drugs. Several published reviews of climate change and food safety suggest that use of veterinary medicines is likely to increase in the coming decades (Boxall *et al.*, 2009; Tirado *et al.*, 2010; Lake *et al.*, 2012) due to increased disease challenges. However, this subject is speculative by nature, data are limited, and other reviewers suggest the evidence base is fragmented and precise prediction of changes to disease load is difficult given the complexity of livestock systems and the myriad interacting factors (Fears & Meulen, 2012; Vermeulen, Campbell, & Ingram, 2012; Thornton, van de Steeg, Notenbaert, & Herrero, 2009).

Pig and poultry production on Iol are almost exclusively indoor, intensive systems and are expected to be insulated from the effects of climate change which might impact veterinary drug use. There is a very small number of extensive, free-range outdoor rearing systems, however these are often organic systems which are less likely to respond to climate-related disease challenges by increasing drug use. Cattle and sheep production on Iol generally follow extensive, outdoor systems and will therefore be more responsive to changes in climate.

One of the few animal diseases which can be clearly linked to changes in climate and is of particular relevance to Iol is infection by helminth parasites (roundworms and flukes). Murphy *et al.* (2006) claim it is the norm for cattle in Ireland to be simultaneously parasitised with a variety of helminths. Consequently, farms on Iol routinely administer significant quantities of anti-helminth drugs (anthelmintics). According to Bennema *et al.* (2010) 59% of

dairy herds in Ireland use preventative anthelmintics compared with 17% in United Kingdom (UK) and 6% in Germany. This high usage is reflected in a study showing that of seven European countries Ireland had the highest incidence of anthelmintic drug residues in locally purchased beef, albeit within permitted limits (Cooper *et al.*, 2012). Application of anthelmintics, usually once or twice per year, is ingrained in the farming culture of Iol and they are one of the most commonly administered veterinary livestock drugs in this region. Given that the aetiology of the parasite infections which require treatment with anthelmintics can be more closely correlated with climate factors than other classes of veterinary drug, a review of this topic forms the core of this article.

Climate change predictions for the island of Ireland

Temperature changes on Iol during the 21st century can now be predicted with a relatively high degree of confidence (Sweeney *et al.*, 2009). Average temperatures will rise by 1.4-1.8°C by 2050 and in excess of 2°C by the end of the century relative to the 1961-1990 baseline. Summer and autumn are projected to warm faster than winter and spring, with the midlands and east of Iol warming more than coastal areas. Rainfall predictions are less certain but represent the most important aspect of climate change which will affect livestock production on Iol. Average rainfall is projected to increase by 10% in winter and reduce by 12-17% in summer by 2050. By the 2080s winter rain will have increased by 11-17% and summer rain reduced by 14-25%. The midlands will be susceptible to the largest winter rainfall increases. The southern and eastern coasts will experience the driest summers, rainfall being reduced by 30-40% by the 2080s. Changes in the frequency of extreme weather events will also be seen. Lengthier heat waves, a substantial reduction in the number of frost days, lengthier rainfall events in winter and more intense downpours in summer are projected. At the same time summer droughts are more likely, especially for eastern and southern regions (Sweeney *et al.*, 2009).

The consequences of climate change are complex with many inter-related variables impacting multi-faceted agricultural production systems. However, grass production underpins many of these systems. It is the most important agricultural crop on Iol and is the main feed source for the sheep, dairy and beef livestock industries. It has been predicted that climate change will not have a catastrophic impact on grassland production in Ireland (Holden & Brereton, 2002). However, regional changes in yields are likely and irrigation may become necessary in the drier east and southeast. Theoretical turnout date of housed animals may come earlier in the season due to higher temperatures but this may be prevented by higher rainfall. Such changes may impact disease dynamics, particularly those affected by stocking density, housing conditions and pasture-dwelling vectors. Changes to something as fundamental as grass growth may therefore lead to changes in administration of veterinary medicines and thus to prevalence of their potentially harmful residues in food.

Political context

Agricultural production on lol has the capacity to enter a new growth phase following reform of the EU Common Agricultural Policy and phasing out of milk quotas by 2015. Both governments on lol (the Republic of Ireland and the United Kingdom) have a vision for the sustainable expansion of livestock production and increasing export trade, as expressed through the Department of Agriculture, Food and the Marine's Food Harvest 2020 report in the Republic of Ireland (ROI) and the Agri-Food Strategy Board's Going for Growth Action Plan 2013–2020 in Northern Ireland (NI). For example, Food Harvest 2020 envisages a 50% increase in milk production and 20% increase in the value of beef products in ROI. Going for Growth aims for a 60% increase in NI agri-food industry turnover by 2020. Such expansion of agricultural production, as it seeks to emulate the burgeoning local food production sector, will see rising numbers of livestock animals and will have to take account of longer term changes in the environment arising from climate change. Assuring the safety of local food production must continue to be of primary concern.

Monitoring food of animal origin for chemical residues arising from veterinary medicines on lol is carried out under EU regulations primarily by the Agri-Food and Biosciences Institute (NI) and Teagasc (ROI) under their National Residues Surveillance Schemes and other testing programmes. Discussions are ongoing within the European Commission to recast Council Directive 96/23/EEC which defines the structure of these schemes across the EU. It is not yet clear what changes this will bring but it is generally believed the new legislation will encourage a more risk-based approach to testing edible tissues for residues. Member States may soon be given more freedom to decide how to target their National Surveillance Schemes.

Potential impacts of climate change on use of veterinary medicines on lol

(i) Anthelmintics

Helminth parasitism

Since parasites of animals are among the main limitations to livestock production and therefore food security (Wall & Morgan, 2009), understanding the effects of climate change on their epidemiology, and consequently their control, is a priority in the face of increasing global food demand.

The main economically important helminth parasites in sheep and cattle in both NI and ROI are the nematodes, *Nematodirus* spp., *Teladorsagia/Ostertagia circumcincta* and *Haemonchus contortus*, as well as the trematodes *Fasciola hepatica* (the liver fluke) and rumen fluke species (*Paramphistomum* spp. and *Calicophoron* spp.). Other nematodes, such as *Cooperia* spp., *Chabertia* spp. and *Oesophagostomum* spp., can be important in some circumstances, but usually as part of a mixed burden (Morgan & van Dijk, 2012).

These debilitating internal parasite infections can cause symptoms such as ill thrift, scouring, anaemia and parasitic bronchitis. Liver fluke disease or fasciolosis limits production in sheep, goats and cattle, with economic losses due to reduced growth and fertility, death and

condemnation of livers at slaughter (Gordon *et al.*, 2013). As well as their effects on meat, milk and wool production, parasites cost the livestock industry many millions of pounds each year due to the costs associated with their control. Fasciolosis alone costs the livestock industry in ROI €90 million and that in NI £50 million per year. Recent estimates place the annual global spend on anthelmintic drugs at more than US \$3 billion (Dalton *et al.*, 2013).

Historically, a seasonality has been evident in parasitic nematode infection. Fig. 1 shows the accepted high risk periods for parasitic disease in young stock, although factors such as changes in climate, management and treatment strategies can affect the occurrence of disease. *Teladorsagia/Ostertagia circumcincta* and *Trichostrongylus* spp. may overwinter on pasture and the numbers of larvae decline in spring. During the early spring months, hypobiotic larvae overwintering in ewes mature and start to produce eggs; an increase in pasture contamination levels occurs over several worm generations, with both adults and young stock contributing to this. The published epidemiology of *Nematodirus* spp. suggests this parasite overwinters as infective larvae in the egg (van Dijk, Sargison, Kenyon, & Skuce, 2010) then, in spring, a mass hatch of eggs is followed by a rapid decline of the larval population. Typically at this time, the pasture is grazed by parasite-naïve animals. The entire *H. contortus* population overwinters in the adult host. Worms mature during the lambing season; female adult worms are highly fecund and pasture contamination builds up rapidly. The relatively high temperature threshold for development of *H. contortus* and the inhibition of developing larvae in hosts in autumn result in a rapid fall in the number of larvae at pasture in the autumn.

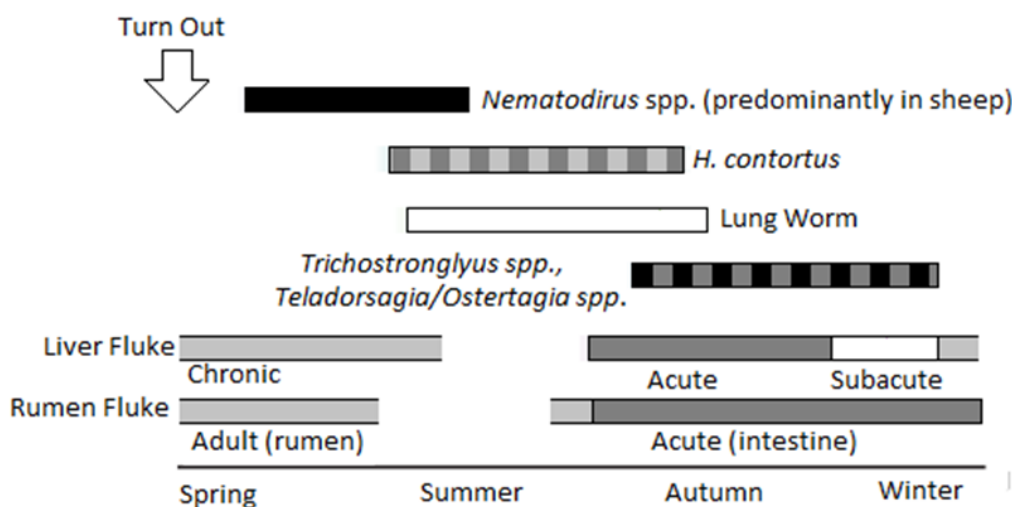


Fig. 1. Classic pattern of the high risk periods for parasitic disease during the calendar year (adapted from Peebles, 2005; van Dijk, Sargison, Kenyon & Skuce, 2010).

The hatching of liver fluke eggs and the multiplication of snails (the intermediate host) depend on adequate moisture and temperatures greater than 10°C. Such conditions usually occur from May to October in the UK, although patterns have been changing in recent years. The incidence of fasciolosis is highest in years when rainfall is above average during May to July. In wet summers, snail populations multiply rapidly and snails are invaded by hatched miracidia from May to July. If wet weather continues, the snails shed massive numbers of

cercariae onto pasture during July to October. Conversely, if the climate in May to July is dry or cold, fewer snails appear, fewer fluke eggs hatch and levels of contamination in the autumn are much lower. Fasciolosis occurs in three main clinical forms: acute, sub-acute and chronic fasciolosis. Which form occurs depends on the numbers of infective metacercariae ingested and the period of time over which they are ingested (Abbott, Taylor, & Stubbings, 2012a). Acute disease occurs from July to December, sub-acute from October to January and chronic disease from January to April.

Paramphistomum cervi was thought to be the predominant species of rumen fluke infecting ruminants in ROI, but it now appears that *Calicophoron daubneyi* is the prevailing species in NI (personal communication). The life cycle of rumen flukes is similar to that of *F. hepatica*, in that it requires two hosts: a mammalian definitive host and a snail intermediate host. *C. daubneyi* and *F. hepatica* are often found as co-infections, share similar life cycles and perhaps even share the same mud snail intermediate host (Skuce & Zadoks, 2013). In the UK it has been suggested that dispersal of snails by flooding events and changes in farm management practices may be responsible for the apparent emergence of the parasite (Foster *et al.*, 2008).

Parasite control: Anthelmintic drugs

Choosing the right anthelmintic drug product and getting the most from it are key factors, not only in the fight against anthelmintic drug resistance, but also in ensuring optimal performance at least cost. However, this can be complicated by the wide variety of brand names, the number of anthelmintic groups, their respective withdrawal periods, their spectra of activity and the development of anthelmintic resistance (Abbott, Taylor, & Stubbings, 2012b).

Anthelmintic products can be considered as having either a broad or narrow spectrum of anti-parasitic activity. Included within the broad spectrum category are:

- the benzimidazoles (BZ), including albendazole, fenbendazole, mebendazole, oxfendazole and ricobendazole
- levamisole (LEV)
- the avermectins (AVMs), including abamectin, doramectin, eprinomectin and ivermectin
- moxidectin (MOX)
- the Amino-Acetonitrile Derivatives (AAD), including monepantel

Products of a narrow spectrum of activity include: clorsulon, closantel, nitroxynil, oxyclozanide and triclabendazole (NOAH, 2013).

Generally speaking, broad spectrum anthelmintics are used to treat lungworm and gastrointestinal nematode infections, while the narrow spectrum products (referred to as flukicide drugs) are predominantly used to treat liver and rumen fluke infections. Exceptions to this generalisation exist and include the use of closantel to treat haemonchosis, as well as fasciolosis, and the use of albendazole to treat fasciolosis, as well as various nematode infections. Combinations of anthelmintics with similar spectra of activity and different mechanisms of action and resistance are available for control of sheep nematodes (Bartram, 2013). Additionally, combinations of broad and narrow spectrum anthelmintics are available. These are formulated to provide broad spectrum control of parasites from different phyla

(nematodes and liver fluke), rather than a mixture of two or more distinct classes of anthelmintics with a similar spectrum of activity to control only one phylum.

One of the main requirements for sustainability of anthelmintic drugs, particularly the macrocyclic lactones (MLs: AVMs and MOX), is the need for guidelines and training for veterinarians and advisors involved in investigating reported treatment failures and suspected anthelmintic resistance. A working group of UK researchers and practitioners devised a set of guidelines in 2003 (Sustainable Control of Parasites in Sheep, or “SCOPS”) aimed at maintaining anthelmintic efficacy on farms. Over the years that followed, these guidelines, now in their fourth iteration, have been promoted through meetings, promotional literature and the agricultural press. Similarly, a technical manual for veterinary surgeons and advisors has been produced with the acronym “COWS” (Control Of Worms Sustainably: Taylor, 2012a), with the intention of shaping effective helminth control programmes for cattle herd owners.

Climate change and helminth parasitism

Climate change (specifically increased temperature and rainfall) will affect the distribution, reproduction, maturation and survival rate of parasites, their vectors and their intermediate hosts (Mas-Coma, Valero, & Bargues, 2009). An increase in the number of generations and expansion of the periods during which conditions are favourable for survival and transmission would be expected to increase potential abundance of endemic parasites. Similarly, warming in temperate areas might enable the spread of more pathogenic species from tropical regions. Therefore, it can be assumed that, as a result of climate change, animals will tend to suffer increasingly high levels of infection.

As well as effects on overall parasite abundance, changes in temporal transmission windows could affect disease risk in a non-linear way by increasing exposure of parasite-naïve animals to infection (Faccini, Santos, & Bechara, 2004), or by increasing nutritional stress as a result of lower digestible protein in grass grown at higher temperatures (Wall, Rose, Ellse, & Morgan, 2011).

While the influence of temperature and moisture on the free-living stages of gastrointestinal nematodes has been described in detail, and evidence for global climate change is mounting, there have been only a few attempts to relate altered incidence or seasonal patterns of disease to climate change. A study of this type has been completed for NI, but not for ROI. The results of the NI study revealed that Trichostrongylosis/Teladorsagiosis predominantly shows a generalised all-year-round distribution, most likely due to high rates of larval survival within the temperature range of NI (McMahon *et al.*, 2012). Considering the seasonal distribution pattern, there was increased incidence of infection in August, as well as higher numbers of cases diagnosed through the autumn to winter months (September to February), indicating a temporal extension of the transmission window, shown in Fig. 2, over the previously described classic pattern (Fig. 1).

While the classic pattern of spring nematodiosis was noted in the findings of the NI study, this was in addition to more significant infection levels detected during the autumn months. This indicates there is a rapid development of eggs in the summer, which are ready to hatch without chilling in the autumn (van Dijk, David, Baird, & Morgan, 2008) and that large-scale hatching of the eggs from spring infections occurs as the average temperatures decline in

the same year (van Dijk & Morgan, 2008). It is conceivable that the late season rise in *Nematodirus* spp. infections has reduced the relative importance of spring nematodirosis, shifting the emphasis towards autumn infections. Any further temperature increase would be expected to exacerbate this shift (McMahon *et al.*, 2012).

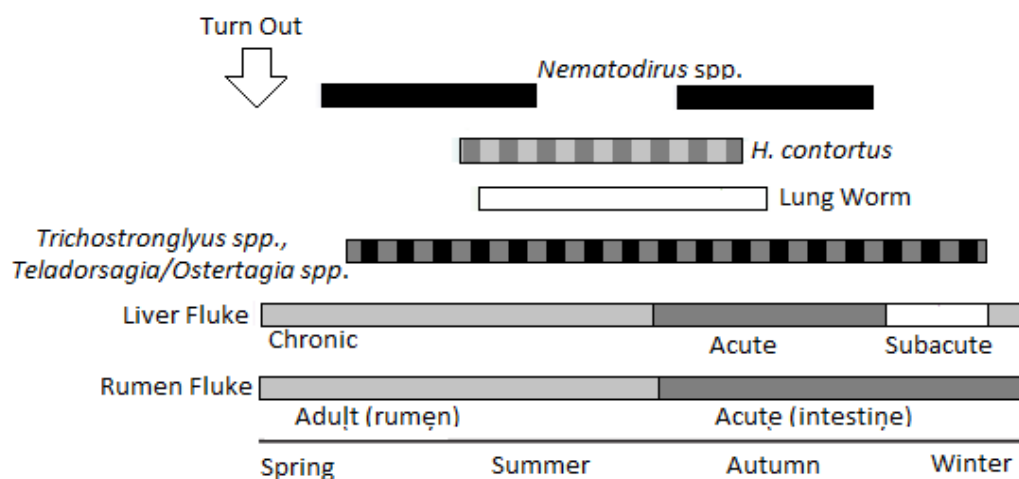


Fig. 2. Current understanding of the high risk periods for infections of parasitic disease over the calendar year (adapted from McMahon *et al.*, 2012).

The observed seasonal, regional and yearly changes in rates of diagnosis may be explained by the effects of rising temperature on parasite transmission. The mean annual temperature has increased in the past 10 years in NI, although the trend is significant for some months only, with temperature increasing earlier and more significantly in February and the following spring months (March to May) than later in the year (McMahon *et al.*, 2012). Higher maximum temperatures during the summer months encourage the accumulation of infective stages from successive generations of adult parasites, increasing parasite abundance and risk of disease. Higher maximum temperatures towards the end of the year, as well as higher minimum temperatures, enhance the ability of larvae to survive on pasture and thus extend the range of larval availability beyond the previously established infection windows. Higher autumn temperatures are likely to increase the proportion of ingested larvae that develop to adults and cause disease in the following weeks, rather than triggering the larvae to enter hypobiosis (or arrested development: van Dijk, David, Baird, & Morgan, 2008).

Over the period investigated (1999–2009), significant decreases in rainfall were detected in April, May and November, while significant increases in rainfall were detected in January to March, September and December. Increased rainfall to the degree shown in NI is predicted to slow the desiccation of faecal deposits, which normally results in the death of the eggs and pre-infective larvae.

The incidence of fasciolosis has risen in recent years, a likely consequence of climate change (Kenyon, Sargison, Skuce, & Jackson, 2009; van Dijk, Sargison, Kenyon, & Skuce, 2010). This trend has been predicted to continue well into the future and the impact of long-term climate changes on the risk of disease in the UK has been estimated (Fox *et al.*, 2011;

Fairweather, 2011a). It is predicted that serious outbreaks of fasciolosis will become the norm in parts of Scotland by 2020 and in Wales by 2050 (Fox *et al.*, 2011). While extreme weather conditions, such as high temperatures, drought and heavy rainfall, may be detrimental to the fluke and its snail host, the authors also point to occasions where high levels of disease followed drought years (Fox *et al.*, 2011). To a certain extent, short-term hostile climatic changes may be cushioned by the longevity of the fluke within its primary host and by infections in reservoir hosts (Kenyon, Sargison, Skuce & Jackson, 2009).

Unfortunately, climate change overlaps with a number of anthropogenic and environmental modifications which are able to give rise to outbreaks of parasitic diseases on their own. Similarly, a major confounding factor in measuring the effects of climate change on parasitism is the rise of anthelmintic-resistant parasite populations (van Dijk, Sargison, Kenyon, & Skuce, 2010). Anthelmintic resistance is currently a major issue in ruminant production in many countries worldwide (Kaplan & Vidyashankar, 2012) and, consequently, constrains sustainable agricultural systems (Fitzpatrick, 2013). Thus, establishing climate change as a cause of disease emergence is not an easy task without an understanding of the anthelmintic resistance status in a given area.

Anthelmintic use and anthelmintic resistance

This section outlines the known usage patterns of anthelmintics to control parasitic diseases on lol and the current knowledge of drug resistance. At the time of writing, no published reports of anthelmintic resistance or parasite control strategies in cattle exist; similarly, information relating to the prevalence of drug resistance in trematode species remains sparse. For information on best practice guidelines for treating parasitic infections, the reader is directed to Abbott, Taylor, & Stubbings (2012c) for sheep and Taylor (2012a) for cattle.

Patten, Good, Hanrahan, & de Waal (2011) carried out a survey of anthelmintic usage on lowland sheep farms in ROI and identified several sub-optimal practices which are known to be selective for anthelmintic resistance. With growing evidence of anthelmintic-resistant parasites in ROI (Good, Hanrahan, & Kinsella, 2003), judicious use of anthelmintics is of paramount importance for the sustainability of production systems. In another recently completed survey, there was evidence of resistance to BZ (on >88% of farms), LEV (>39%) and suspected ivermectin resistance (11%), although these figures need to be confirmed (Good *et al.*, 2012). *T. circumcincta*, *Trichostrongylus* spp. and *Cooperia* spp. were the main species identified.

The current status of anthelmintic resistance in liver fluke in ROI is less well known. In a comparative study of the efficacy of four anthelmintics in a hill flock in the west of Ireland, oxclozanide, closantel and nitroxynil were still fully effective, while triclabendazole efficacy was reduced by approximately half (Mooney *et al.*, 2009).

In NI, resistance to the available anthelmintic classes was recently recorded as prevalent in 81% of flocks tested for BZ resistance, 14% of flocks tested for LEV resistance and in 50% and 62% of flocks tested for AVM and MOX resistance, respectively. AAD resistance was absent in all flocks tested (McMahon *et al.*, 2013a).

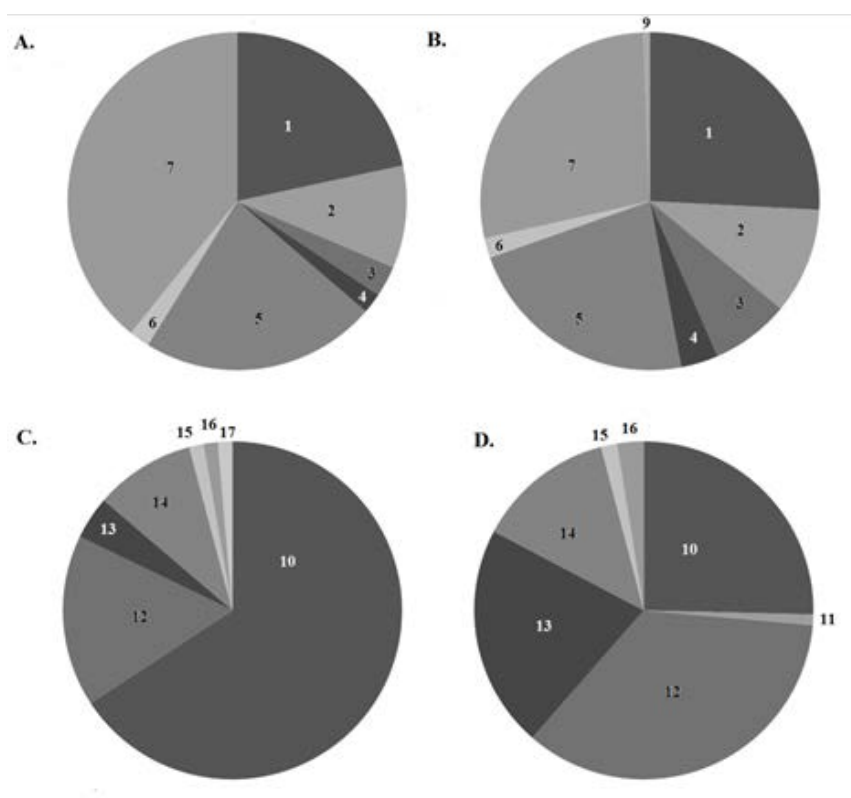


Fig. 3. Average proportions of anthelmintic products used to treat nematode infection over the periods 2000–2005 (A) and 2008–2011 (B) and trematode infections over the same periods (C and D, respectively). Products containing: 1 = Benzimidazoles; 2 = Benzimidazoles*; 3 = Levamisole; 4 = Levamisole*; 5 = Avermectin; 6 = Avermectin*; 7 = Moxidectin; 8 = Moxidectin*; 9 = Amino-acetonitrile derivative (N.B. only available since 2008); 10 = Triclabendazole; 11 = Triclabendazole*; 12 = Closantel; 13 = Closantel*; 14 = Nitroxynil; 15 = Oxytoclozanide*; 16 = Albendazole; and 17 = Clorsulon (* denotes product delivered in combination formulation).

Between 2005 and 2011, a number of changes in sheep management practices in NI were identified (McMahon *et al.*, 2013c) which would be expected to slow the spread of anthelmintic resistance. These included increased duration of quarantine separation and increased contribution to the *in refugia* population by ewes. The *in refugia* population is a population of parasites unexposed to drug treatment and is most commonly found in untreated hosts. Between 2008 and 2011, annual rotation between flukicide drug groups was practiced by 30% of flock owners, with 24% rotating with each successive treatment and the remaining 46% opting to use the same product in successive years, allowing repeated exposure of the parasite population to the same anthelmintic compounds. These figures are an improvement over the corresponding figures from 2000 to 2005 (10%, 8% and 83% respectively). However, a number of practices which are selective for anthelmintic resistance are still commonly used in NI. These include using unchecked dosing equipment, co-grazing sheep and cattle, always using the same anthelmintic product and a decreasing contribution to the *in refugia* population by lambs (McMahon *et al.*, 2013b).

Relatively little is known about the levels of triclabendazole resistance in NI; this reflects both the lack of large-scale surveys and the lack of universally accepted criteria for the declaration of flukicide resistance (Fairweather, 2011b). Preliminary observations suggest a

prevalence of 38% resistance in NI (unpublished data). However, the perception in the farming community is that triclabendazole resistance is widespread and this is reflected in the reduction of triclabendazole use from 67% by 2005 to 26% by 2011 (Fig. 3). This gap has largely been filled by closantel, either as a single active or in combination with ivermectin, its use increasing from 22% by 2005 to 56% by 2011 (McMahon *et al.*, 2013b). Closantel's popularity is demonstrated by it being the most common anthelmintic residue detected in a survey of beef purchased in ROI in 2009–2010 (Cooper *et al.*, 2012).

The rise of LEV use between 2000–2005 and 2008–2011 (Fig. 3) may reflect the suggestion that it is used in the treatment of quarantined animals, or that it remains a functional alternative to the MLs in the face of increasing ML resistance. The greater use of LEV in combination products is likely due to the increased awareness of rumen fluke; for example, at the time of writing, the only products licensed in the UK for the treatment of rumen fluke are those which combine the salicylanilide oxyclozanide with LEV.

Product selection is influenced heavily by price, method of application and a history of effective use (Patten, Good, Hanrahan, & de Waal, 2011; McMahon *et al.*, 2013c). Increasing levels of anthelmintic resistance (confirmed or anecdotal accounts), therefore, will have an effect on product selection which, in turn, will have an effect on when the meat or milk produced will be suitable for human consumption, given that different anthelmintic products are subject to different withdrawal periods.

The anthelmintic challenge to be faced

Recent years have seen the release of new anthelmintics, namely, the AADs (Zolvix®) and the release of the first multiple-active formulation (in the UK). However, there are no more new anthelmintics on the horizon and evidence suggests that resistance emerges within a relatively short time period (<10 years) following the commercial release of a new anthelmintic compound (Kaplan, 2004). Reports of resistance to MLs are increasing in frequency in NI and elsewhere in the UK (Bartley *et al.*, 2012; Jones, Pearson, & Jeckel, 2012; Stubbings, 2012; McMahon *et al.*, 2013a). It is clear that effective parasite control in the future requires action in the present to increase awareness of best practice procedures to minimise the spread of resistance and the occurrence of drug residues in livestock produce.

To a large extent, farmers on lol do not seem to be following the published SCOPS/COWS guidelines (Patten, Good, Hanrahan, & de Waal, 2011; McMahon *et al.*, 2013c). Already there have been large-scale shifts in product use (Fig. 3) and changes in treatment timing (McMahon *et al.*, 2013b; unpublished observations). These changes in timing are linked to the withdrawal periods of products, the perception of resistance, the spectra of activity of the products and the altered seasonal appearance of parasites (Figs. 1 and 2). These alterations have not arisen through the emergence of anthelmintic resistance alone, but as a result of a combination of factors. Such factors include more favourable climatic conditions for the completion of the parasites' life cycles, large-scale movements of livestock and their parasites following the Foot and Mouth Disease outbreak in the UK and farmers being encouraged to retain or introduce wetlands into farming systems as part of environmental programmes (Skuce & Zadoks, 2013).

The future of helminth parasite control

Renewed appreciation of the influence of climate on the epidemiology of helminth parasites is essential. With a sufficient level of knowledge, it will be possible to:

- predict the main times of infection and intervene accordingly
- track the fate of eggs produced by drug-resistant nematodes and ensure adequate dilution *in refugia*
- model the effects of climate change and build rational strategic and farm level responses accordingly (Morgan & van Dijk, 2012)

Any response to increased parasite challenge that relies on increasing anthelmintic drug use is likely to be self-defeating through the further development of drug resistance. This applies to targeted treatments as well as generally increased treatment frequency in summer.

Future sustainable control strategies for helminth resistance to anthelmintics require an integrated approach, including environmental management, taking into account the climate and species of parasites in different areas, as well as chemoprophylaxis to minimise the pressure for parasite adaptation (Papadopoulos, 2008). Meteorological data to predict the prevalence of parasitic disease is compiled and released annually by organisations such as NADIS (National Animal Disease Information Service) and the Agri-Food and Biosciences Institute in NI, for both *Nematodirus* spp. infection and fasciolosis. These forecasts provide an indication of the best times to treat for the respective helminthoses. Together with the guidelines to slow the development of resistance, such measures will be vital in shaping the future of livestock production, which has to face the challenges of continuing climate change, minimising anthelmintic drug residues and ensuring food safety.

(ii) Other endoparasiticides

Babesiosis is a parasitic infection caused by protozoa of the genus *Babesia* leading to lysis of the red blood cells. It is spread via ticks and is a significant disease of cattle, although its incidence in Ireland has declined markedly in recent years (AFBI, 2012). The “castor bean tick”, *Ixodes ricinus*, is the only tick which affects Irish livestock. It has been suggested that climate change may increase the geographical range of ticks in Western Europe (they favour mild, moist conditions) with a consequent increased incidence of babesiosis (Hasle *et al.*, 2010). Increased use of babesiosis chemotherapies such as imidocarb is therefore possible and residue monitoring programmes should be alert to changing patterns of use.

(iii) Ectoparasiticides

Livestock are also susceptible to infestation by ectoparasites. Sheep are particularly vulnerable to external parasitic conditions such as blowfly strike, sheep scab (*Psoroptes ovis*), and ticks, lice, mites and keds. Treatments generally involve pour-on products or, to a lesser degree, dipping in synthetic pyrethroid or organophosphorus compounds, although concerns over toxicity to the farmer and the environment persist. Ectoparasite infestations are also treated with injectable macrocyclic lactones.

Treatment with pour-on and dipping products can be considered food safety issues since pyrethroid residues can be detected in edible tissues, and meat is monitored routinely to ensure compliance with maximum residue limits, as is also the case with macrocyclic lactones.

Climate warming is predicted to have profound effects on the incidence of blowfly strike in Great Britain (Rose & Wall, 2011) through faster blowfly development, increased numbers of generations and prolonged periods of favourable conditions for fly survival. A warmer climate may also affect strike incidence indirectly through changes to the seasonal pattern of sheep susceptibility and the timing of seasonal farm management practices (Wall, Rose, Ellse, & Morgan, 2011). Conversely, lice infestations tend to be worse in cooler seasons, so climate change is unlikely to make veterinary treatment more common. By contrast, climate change is thought to have already affected the epidemiology and geographical distribution of tick infestations making them more prevalent (Taylor, 2012b). However, precise prediction of climate effects on the incidence of ectoparasite infestations is uncertain due to subtle and conflicting interactions of humidity and temperature, free-living and host-bound life stages, and indirect effects on the host species and husbandry practices (Wall, Rose, Ellse, & Morgan, 2011, Morgan & Wall, 2009). Indeed, one recent Europe-wide model predicts less favourable conditions for tick survival on lol by 2050, but improving conditions by 2080 (Porretta *et al.*, 2013). Nevertheless, climate change raises the possibility of changing patterns of veterinary drug administration to combat ectoparasites with consequent potential for impacts on residues in edible tissues.

(iv) Antibiotics

A variety of veterinary antibiotics are used therapeutically to treat a wide range of bacterial diseases and secondary infections in livestock. They are also used to control established outbreaks of disease and to prophylactically protect animals considered to be at risk of infection. Since 2006 the use of antibiotics as growth promoters in EU livestock has been banned. Climate change may, via various routes, have adverse impacts on bacterial livestock diseases which can be treated with antibiotics.

(a) *Changes to ground conditions*: Increased flooding and waterlogged ground (likely consequences of climate change on lol) have the potential to increase endemic bacterial animal diseases spread via the faecal-oral route (reservoirs of infective bacteria in the soil and faeces), although survival of pathogens in the environment is typically less in warmer conditions (Gale *et al.*, 2009). Salmonellosis, calf diphtheria, listeriosis, leptospirosis, tetanus, enzootic abortions, stiff lamb disease and others could become more common, requiring enhanced antibiotic treatments. Cases of botulism and anthrax may even increase (Gale *et al.*, 2009); however, with slaughter being the primary control policy rather than chemotherapy for such serious diseases (as also for bovine tuberculosis and brucellosis), these latter do not *per se* represent an enhanced chemical food safety risk. Populations of rodents carrying bacterial diseases may be displaced by flooding, changing the dynamics of transmission to livestock. Poorer ground conditions may also lead to more livestock hoof problems and lameness requiring antibiotic treatment for foot rot and digital dermatitis.

(b) *Vector-borne bacterial infections*: Tick infestations may increase as their favourable seasonal periods of mild, moist conditions lengthen. Tick-borne bacterial diseases such as

tick-borne fever (a common but largely unrecognised and untreated infection), tick pyaemia, Q fever, anaplasmosis and Lyme disease may become more common and antibiotic treatments may rise. Lyme disease, caused by *Borrelia burgdorferi*, is strongly associated with deer populations (which are growing on lol) and is rarely diagnosed and symptoms may be minor in livestock. However, its impact may grow if climate change alters tick prevalence and brings deer and livestock populations into closer proximity.

(c) *Weather conditions*: The epidemiologies of many bacterial diseases are influenced by the interplay of temperature and humidity. The predicted warmer, wetter weather on lol may be conducive to increased cases of mastitis in cattle and dermatophilosis (lump wool) in sheep. In regions where warmer and drier conditions are forecast, cases of keratoconjunctivitis (pink eye) may increase where dust and flies are predisposing factors in the summer months. Wetter conditions in the colder months could potentially lead to more cases of pneumonia in calves and pasteurellosis (enzootic pneumonia) in sheep, particularly if routine handling practices are disrupted. Furthermore, if climate change encourages the intensification of production, for example housing animals more frequently to avoid bad weather, more cases of atypical pneumonia in sheep and other diseases of intensification may be seen. In addition to bacterial diseases, toxoplasmosis in sheep (caused by the protozoan *Toxoplasma gondii*) also responds to sulphonamide antibiotic treatment, although vaccination is the preferred approach. As described below for coccidial infections, predicted warm, wet weather may assist the survival of the infective oocysts in faeces and grass and may lead to an increase in toxoplasmosis-related abortions. More frequent administration of antibiotics or preventative coccidiostat drugs may follow.

The degree to which such theoretical changes to disease dynamics will actually occur is difficult to predict, since there will be other drivers in the coming decades (e.g. changing husbandry practices) which may mitigate their effects. Furthermore, increased drug administration may not automatically follow increased disease prevalence – this will always depend on the economic viability of using extra veterinary medicines. However, the above list serves to illustrate the possible wide ranging effects of climate change on antibiotic drug use and the need to ensure that testing schemes for drug residues in food are maintained and remain adaptable to changing on-farm practices.

(v) Antiviral drugs

Livestock are susceptible to a range of viral diseases with major welfare and economic impacts. Research into treatment of viral livestock diseases has largely focused on development of vaccination programmes, with variable success. For example, thanks to vaccination and control programmes initiated in the 1980s, several European countries are now officially free of Aujeszky's disease, a contagious and lethal viral disease of pigs. However, vaccines are available only against limited serotypes of the Bluetongue virus, highlighting the difficulty of ongoing protection via vaccination as viruses mutate and different strains become prevalent in subsequent years. As was the case with the Foot and Mouth Disease outbreak in the UK in 2001, whilst effective vaccines were available, widespread isolation and culling of infected animals is often required in the event of viral disease outbreaks, as vaccination can be prohibitively expensive or may provide incomplete protection. Sales in ROI of veterinary preventative vaccines for farm animal species grew by

over 80% between 2007 and 2011 indicating a growing acceptance within the farming community of preventative approaches to livestock health (AFBI, 2012).

Whilst vaccination, husbandry control measures and culling have been the traditional approaches to dealing with viral diseases in livestock, research also focuses on the development of innate resistance through breeding programmes. Beyond these varied approaches, the use of antiviral drugs to treat infected animals is controversial. Antiviral drug treatments have generally been limited to companion animals, but have potential for wider application to livestock.

The highly pathogenic and zoonotic H5N1 strain of the avian influenza virus became widespread during 2003–2004, spreading from Asia to Europe resulting in millions of poultry infections and several hundred human cases. In the wake of these outbreaks and reports of prophylactic use of antiviral drugs in poultry flocks in Asia, the FAO, OIE and WHO jointly urged Member States in 2005 *“not to use antiviral drugs in animals in order to preserve the efficacy of these drugs for the treatment of influenza infections in humans. They strongly request Member States to ban the use of antiviral drugs in animals”* (WHO, 2005). Analytical methods have been developed to test for residues of some antiviral drugs in poultry meat (Berendsen *et al.*, 2012), but widespread adoption of antiviral drugs by livestock industries has thus far been averted. Residues of antiviral drugs do not currently form a part of routine residues testing plans in Europe.

Yet the use of antiviral drugs in combination with other control strategies has been proposed as the most efficacious and cost-effective means of eradicating some viral disease outbreaks such as classical swine fever in countries with high density livestock (Wageningen University and Research Centre, 2012). If greater therapeutic use is made of existing antiviral drugs or new drugs are developed specifically for livestock diseases, further toxicological assessment of the risk posed by residues entering the human food chain would be necessary.

Climate change will undoubtedly have a significant influence on emerging vector-borne viral diseases in Western Europe (Gale *et al.*, 2009). This has already been demonstrated by the northward expansion of the Bluetongue virus from Africa to Southern Europe (causing a non-contagious disease of ruminants with variable symptoms), although whether climate change is responsible for its subsequent appearance in Western Europe in 2006 is debatable (Paul-Pierre, 2009). Bluetongue is transmitted by biting *Culicoides* midges and Iol is currently free of the disease following an isolated appearance in 2008 via importation of cattle from Europe. Similarly, the Schmollenberg virus, also transmitted via midges, causing abortions or premature births with congenital deformity in sheep and cattle, appeared in Western Europe in 2011. The spread of midges and other virus vectors such as ticks (vector for Louping ill in sheep, for example) may be significantly affected by the changes in climate predicted for North-western Europe. If significant animal viruses become endemic on Iol, there may be pressure to use antiviral drugs on a routine basis for both economic and animal welfare reasons or to increase usage of acaricide drugs to kill ticks and other virus vectors. The possibility of harmful residues in food would then be an issue, possibly requiring new toxicological assessments, setting of legislative limits and implementation of testing plans to ensure food safety. Such developments would be subject to the continuing tensions between clinical human and veterinary concerns. It is to be hoped that the painful lessons currently being learned from the long-term use of antibiotic compounds in livestock

production (that is, the development of drug resistant bacteria capable of infecting the human population) will be heeded should the potential arise for widespread use of livestock antiviral drugs.

(vi) Anti-inflammatory drugs

Whilst steroid hormones have been banned in the EU for livestock growth promotion, some corticosteroids (for example, dexamethasone) are licensed for veterinary use, primarily for anti-inflammatory purposes and treatment of ketosis in ruminants. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are a large group of chemically heterogeneous drugs which are used in livestock to control pain and suppress inflammation in a manner similar to steroids but with fewer side effects. They are used primarily in cattle, horses and pigs to treat a wide range of infectious conditions including coliform (environmental) mastitis, respiratory disease, lameness and joint infections. Veterinary surgeons may also use NSAIDs before surgical procedures or after calving a cow. They are also effective in reducing acute pain associated with castration and disbudding/dehorning but are not often administered because of cost and lack of perceived need for pain relief. NSAIDs are rarely used to treat sheep for similar reasons and lack of licensed products (NADIS, 2013).

It is conceivable that climate change may indirectly lead to increased incidences of lameness and joint infections in livestock due to changes in ground conditions and stock movements resulting from the predicted increases in isolated flooding and waterlogged land on lol. Furthermore, the predicted warmer and wetter climate may be conducive to increased bovine coliform mastitis (Hogan & Smith, 2003) and respiratory infections (Tirado *et al.*, 2010), treatment of which often include anti-inflammatory drug administration alongside appropriate antibiotics. It is therefore possible that administration of anti-inflammatory drugs will increase in coming years and residues monitoring plans will need to be effective in preventing any increased food safety risk.

(vii) Coccidiostats

Veterinary drugs which combat coccidiosis in livestock (a protozoal disease caused by parasites of the genus *Eimeria*) are used most heavily in intensive indoor rearing systems (Kools *et al.*, 2008), particularly the poultry and pig industries. Indoor rearing systems are expected to be largely insulated from the effects of climate change due to their biosecurity measures (Gale *et al.*, 2009) and should see little appreciable change in veterinary drug use as a result of this driver. Other drivers (economics, drug resistance issues, welfare concerns) will have larger impacts on the use of anticoccidial drugs in intensive agricultural systems.

Cattle and sheep production on lol generally follow extensive, outdoor systems. Anticoccidial drugs may also be used for therapeutic treatment of scouring (severe diarrhoea) in calves and lambs, sometimes in tandem with preventative drugs (primarily halofuginone) against *cryptosporidia*, one of the most common causes of scouring. Broad spectrum antibiotics may also be administered to young animals exhibiting severe symptoms of scouring to prevent bacteraemia or septicaemia. However, whilst drug treatments may be employed, the primary responses to scouring in extensive rearing systems are reactive (separate and rehydrate the calf) and preventative animal management practices (addressing bedding, cleaning and stocking density issues) rather than drug administration (AHI, 2011).

Climate change has the potential to increase the incidence and distribution of parasitic diseases, including coccidiosis, in animals reared outdoors (Taylor, 2013). Warm and moist conditions provide the optimal environment for development (sporulation) of the infectious protozoa oocysts in contaminated faeces, grass or feed, which may then be ingested by young, vulnerable animals. Predicted climatic changes in lol, that is, higher temperatures and more frequent rainfall, are likely to increase the disease challenge to livestock in the peak seasonal period of coccidiosis in spring. Coccidiosis in lambs at pasture is already a problem in the UK with increased stocking density and reduced availability of pasture for sheep (Taylor, 2012b). A young animal's resistance to coccidial infection can also be reduced by various stress factors which can include extreme temperature and weather conditions (Taylor, 2012b). Whilst extreme weather fluctuations are an accepted consequence of global climate change, it remains to be seen if lol will experience sufficient dramatic oscillations in temperature and rainfall to cause significant increased stress to young livestock in the field.

Climate change therefore has the potential to increase the need for administration of various licensed veterinary medications to treat coccidiosis and cryptosporidiosis in livestock reared outdoors or in open sheds. However, given that such infections, often leading to scouring, are primarily treated in young animals, increased drug use may not necessarily represent an increased food safety risk in the form of harmful drug residues, since sufficient withdrawal periods will have been observed prior to slaughter some months later.

(viii) Drug residues in the environment

The occurrence, fate and persistence of veterinary drug residues and their subsequent effects in the environment is a growing area of research which may still be considered to be in its infancy (Kemper, 2008). It is estimated that, depending on the product, 30–90% of the antimicrobial compounds administered to livestock are excreted unaltered or as active biotransformation products. These residues can enter the environment, contaminating land and waterways either directly through faeces and urine from grazing animals, or indirectly through routine application of manure and slurry to agricultural land as fertilisers. Pharmaceuticals used in human medicine may also find their way onto agricultural land via the recycling of waste water in irrigation systems and application of biosolids (sewage sludge) as agricultural fertiliser (Monteiro & Boxall, 2009). Such use of biosolids in agriculture is encouraged by official Codes of Practice on lol as *“the most sustainable option of sludge management”* and providing *“both the macro and micro nutrients required for healthy plant and animal growth”* (DECLG, 2008). However, biosolids fertilisation is not widespread on lol as only a small percentage of agricultural land is required to dispose of the currently available material from human waste treatment plants.

Research into the subsequent effects of veterinary and human pharmaceutical residues in the environment has focused largely on the evolution of antimicrobial resistant organisms and the deleterious effects on ecosystems, with aquatic systems receiving more attention than terrestrial systems (Du & Liu, 2012; Arnold *et al.*, 2013). Antibiotics and parasiticides (including anthelmintics) have been ranked as the European veterinary medicines most likely to pose risks to the environment (although anticoccidial drugs pose a high risk within intensive rearing systems) and worthy of further risk assessment (Kools *et al.*, 2008). Concentrations of residues in the environment are not regulated despite estimates that the

shedding of antibiotics via manure may be up to kilograms per hectare (Kemper, 2008). It has been suggested that environmental risk assessments of human pharmaceuticals and veterinary medicines should be approached differently due to the differing nature of their release into the environment: human pharmaceuticals can be considered to be pseudo-persistent contaminants due to their continuous release from wastewater treatment plants, whilst release of veterinary medicines is likely to be more sporadic (Brooks, Huggett, & Boxall, 2009).

The recycling of environmental pharmaceutical residues back into the human food chain and the consequent food safety issue this implies have received little attention from researchers. Drug residues are known to accumulate in soils but their degradation routes are complex and data are limited (Monteiro & Boxall, 2009). Residues are also detectable in agricultural run-off water (MacKie *et al.*, 2006) and urban wastewaters due to the incomplete removal of pharmaceuticals in wastewater treatment plants. Research continues into methods of removal of veterinary drug residues from the environment, such as the planting of reed beds (Carvalho, Basto, & Almeida, 2012). The uptake of veterinary drugs from contaminated soils and water by plants has been demonstrated (Chitescu, Nicolau, & Stolker, 2013; Boxall *et al.*, 2006; Brooks, Huggett, & Boxall, 2009). For example, nitrofurantoin antibiotic residues were detected in grass from a paddock occupied by free-range chickens which had inadvertently received the drug in their water (McCracken & Kennedy, 2013). The residues were bound to the grass matrix, demonstrating this was not simple surface contamination via litter.

The accumulation of pharmaceuticals in crops raises food safety issues for human consumers of those plants (Du & Liu, 2012) but the question remains whether residues from plants are detectable in tissues or produce of livestock which have eaten the crops. It has been suggested there is a need for risk assessment of the exposure of humans to pharmaceuticals in food which arises from environmental uptake rather than direct application to crops or livestock. Such assessments ought to consider longer term exposure and effects on sensitive human sub-populations (Brooks, Huggett, & Boxall, 2009).

It is reasonable to assume that climate changes could influence the uptake of environmental drug residues into plants and their subsequent release into animal tissues, but the extent of the health risk to consumers is unclear. It is thought that whilst this contamination route is viable, the risk to human health will be low (Kennedy, Cannavan, & McCracken, 2000; Boxall *et al.*, 2006; McCracken & Kennedy, 2013), particularly if mediated via large animal species, and is of much lesser concern than the ongoing direct application of veterinary medicines to livestock (Balbus *et al.*, 2013). Nevertheless, reduction in emissions of antibiotics into the environment is desirable (Kemper, 2008) and composting and digestion are well-established methods for reducing antibiotics in manures (Du & Liu, 2012). Further study of the mechanisms of uptake into plants and soils is warranted (Boxall *et al.*, 2006) in addition to risk assessment of pharmaceuticals and their metabolites in soil-crop systems (Du & Liu, 2012). Exposure assessments will be affected by water availability (Arnold *et al.*, 2013) and therefore by climate-driven changes in rainfall on lol.

Conclusion

Many factors influence the emergence of animal diseases and their subsequent treatments which may lead to harmful drug residues persisting in food. As reviewed by Gale *et al.* (2009) in the Great Britain context, there is strong evidence to suggest climate change will continue to have a major impact on animal disease occurrence and prevalence. However, precise forecasting of disease emergence is problematic. Its status as an island may partially protect lol from climate-driven changes to animal diseases, but this may simply be delaying the inevitable as global warming is likely to continue. Animal transportation (importation of diseased stock) will continue to be a major route for emerging infections on lol.

Climate change on lol is likely to increase the disease burden on some agricultural livestock. With the exception of parasitic helminth infections, there is little published data on the subject, but it is likely the changes will not be extreme. Nevertheless, administration of veterinary medicines to food animals is likely to increase, although distinguishing climate change effects from other drivers is difficult. For example, encroaching drug resistance may lead to administration of greater quantities of medications or alternative drugs being used inappropriately. Overall, there is the potential for more and different residues of veterinary medicines to appear in locally produced foods over an extended period. Existing food safety control measures on lol will need to be sufficiently flexible to identify changes in the profile of veterinary residues and preclude their entry into the marketplace.

Global efforts to mitigate anthropogenic climate changes have focussed largely on reducing emissions of greenhouse gases in an effort to reduce the rate of global warming. Livestock production systems are estimated to account for around 8% of emissions in the UK, and 18% globally (Gill, Smith, & Wilkinson, 2010). Whilst livestock producers on lol must do their part in mitigating adverse climate change effects by reducing greenhouse gas emissions during food production, such efforts in one small region will not in themselves prevent the predicted climate changes on this island.

However, the following mitigation and adaptation strategies can be implemented at a local level and are suggested to ensure that predicted climate change on lol does not adversely affect food safety via increasing veterinary drug residues.

Mitigation strategy: Reducing veterinary drug use

Reducing the use of veterinary drugs is the most effective way of guarding against climate change-driven increases in harmful residues in food.

- *Developing alternative treatments:* Resourcing fundamental research and development into alternatives to existing drug treatments will pay long-term dividends. Primary examples include production of vaccines against helminth infections and bacteriophage therapy as an alternative to livestock antibiotics.
- *Educating farmers and producers:* Livestock management practices which reduce drug usage should be promoted to primary producers. Examples include *in refugia* (Charlier *et al.*, 2012) and grazing strategies (Colvin, Walkden-Brown, Knox, & Scott, 2008) to control helminth infections. The message of appropriate use of effective veterinary medicines must continue to be driven home to avoid

unnecessary administration of drugs which can lead to animal welfare issues, greater residues in food and increasing drug resistance.

Adaptation strategies

(i) Enhancing residues monitoring

Iol is fortunate to have chemical residues testing laboratories with international reputations which regularly perform to the highest standards in EU proficiency tests for veterinary drug residues and are in the forefront of research and development in this field. Multi-analyte residue detection methods are constantly being implemented in the residues laboratories in both jurisdictions using state-of-the-art mass spectrometric equipment in addition to a range of rapid screening procedures. As required by EU legislation, extensive residue monitoring programmes are in place and additional testing schemes are ongoing to protect Iol produce and consumer safety.

To ensure that climate change does not adversely affect food safety, sufficient resources must continue to be in place to expand the scope of this testing. For example, as veterinary drugs succumb to increasingly resistant microbe and parasite strains, less common drugs may gain in popularity with producers. Testing schemes must encompass relevant new and emerging veterinary drugs and take account of the possibility of increased usage of existing drugs as disease loads on livestock increase as a result of climate change.

With changes imminent to EU legislation governing residues testing, it is likely that National Residues Surveillance Schemes will be adapted to a more targeted, risk-based sampling approach. Should risk assessment become integral to food safety testing regimes on Iol, the risks associated with climate change as described above must be taken into account and resources made available to gather the necessary data.

(ii) Filling the knowledge gaps

- *Veterinary drug usage:* There is a need for reliable, quantitative, data defining the types and amounts of veterinary medicines used in food production on Iol. Currently only limited sales figures or producer questionnaires are available. Further information is required to track changes in drug applications in coming years.
- *Veterinary drug residues in the environment:* There is a need for comprehensive research to quantify veterinary residues in the environment and the extent to which they are recycled back into the human food chain.
- *Environmental residues and resistance:* There is a need for fundamental research on the relationship between veterinary drug residues in the environment and the occurrence of drug resistant target species (Kemper, 2008) to determine if there is a link, if there are critical threshold concentrations and if the link can be circumvented (Call, Matthews, Subbiah, & Liu, 2013).

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